WHAT IS CLAIMED IS:

1. An isolated $GABA_B$ receptor protein comprising at least one $GABA_BR1a$ subunit and at least one $GABA_BR2$ subunit, characterized in that said $GABA_B$ receptor has one high affinity agonist binding site and one low affinity agonist binding site.

2. The $GABA_B$ receptor protein according to claim 1 wherein the $GABA_BR1a$ subunit is encoded by the oligonucleotide sequence consisting of SEQ ID No.1 and the $GABA_BR2$ subunit is encoded by the oligonucleotide sequence consisting of SEQ ID N0.3.

3. The $GABA_B$ receptor protein according to claims 1 or 2 wherein said receptor protein is expressed by the $hGABA_BR1a/GABA_BR2$ CHO cell line deposited at the Belgian Coordinated Collections of Microorganisms (BCCM) as CHO-K1 h-GABA-b R1a/R2 clone 20 on August 22, 2003 with the accession number LMBP 6046CB.

4. Use of the $GABA_B$ receptor protein according to any one of claims 1 to 3 in a method to identify $GABA_B$ receptor agonists or antagonists.

5. The $hGABA_BR1a/GABA_BR2$ CHO cell line deposited at the Belgian Coordinated Collections of Microorganisms (BCCM) as CHO-K1 h-GABA-b R1a/R2 clone on August 22, 2003 with the accession number LMBP 6046CB.

6. A method to identify whether a test compound binds to a $GABA_B$ receptor protein according to any one of claims 1 to 3, and is thus a potential agonist or antagonist of the $GABA_B$ receptor, said method comprising:

a) contacting cells expressing a functional $GABA_B$ receptor, wherein such cells do not normally express the $GABA_B$ receptor, with the test compound in the presence and absence of a compound know to bind to the $GABA_B$ receptor, and

b) determine the binding of the test compound to the $GABA_B$ receptor using the compound known to bind to the $GABA_B$ receptor as a reference.

7. A method according to claim 6, wherein the compound known to bind to the $GABA_B$ receptor is detectably labeled, and wherein said label is used to determine the binding of the test compound to the $GABA_B$ receptor.

8. A method according to claim 7 wherein the compound known to bind to the $GABA_B$ receptor is selected from the group consisting of ^{3}H-GABA, ^{3}H-baclofen, ^{3}H-3-APPA, ^{3}H-CGP542626 and ^{3}H-SCH50911.

9. A method to identify $GABA_B$ receptor agonists said method comprising,

a) exposing cells expressing a functional $GABA_B$ receptor, wherein such cells do not normally express the $GABA_B$ receptor, to a labeled agonist of $GABA_B$ in the presence and absence of the test compound, and

b) determine the binding of the labeled agonist to said cells,

where if the amount of binding of the labeled agonist is less in the presence of the test compound, then the compound is a potential agonist of the $GABA_B$ receptor.

10. A method according to claim 10 wherein the labeled agonist is selected from the group consisting of ^{3}H-GABA, ^{3}H-baclofen and ^{3}H-3-APPA.

11. A method to identify $GABA_B$ receptor antagonists said method comprising,

a) exposing cells expressing a functional $GABA_B$ receptor, wherein such cells do not normally express the $GABA_B$ receptor, to a labeled antagonist of $GABA_B$ in the presence and absence of the test compound, and

b) determine the binding of the labeled antagonist to said cells,

where if the amount of binding of the labeled antagonist is less in the presence of the test compound, then the compound is a potential antagonist of the $GABA_B$ receptor.

12. A method according to claim 10 wherein the labeled antagonist is selected from the group consisting of ^{3}H-CGP542626 and ^{3}H-SCH50911.

13. A method for identifying a compound as a $GABA_B$ receptor agonist, said method comprising;

a) administering the compound to a cellular composition of the cells according to claim 5, in the presence of a detectably labeled $GABA_B$ receptor agonist; and

b) determine the binding of the labeled agonist to said cellular composition,

where if the amount of binding of the labeled agonist is less in the presence of the test compound, then the compound is a potential agonist of the $GABA_B$ receptor.

14. A method according to claim 13 wherein the cellular composition consists of a membrane fraction of the cells according to claim 5.

15. A method according to claims 13 or 14 wherein the labelled agonist is selected from the group consisting of ^{3}H-GABA, ^{3}H-baclofen and ^{3}H-3-APPA.

16. A method for identifying a compound as a $GABA_B$ receptor antagonist, said method comprising;

a) administering the compound to a cellular compositon of the cells according to claim 5, in the presence of a detectably labeled $GABA_B$ receptor antagonist; and

b) determine the binding of the labeled antagonist to said cellular composition,

where if the amount of binding of the labeled antagonist is less in the presence of the test compound, then the compound is a potential antagonist of the $GABA_B$ receptor.

17. A method according to claim 16 wherein the cellular composition consists of a membrane fraction of the cells according to claim 5.

18. A method according to claims 16 or 17 wherein the labeled antagonist is selected from the group consisting of ^{3}H-CGP542626 and ^{3}H-SCH50911.

19. A method for identifying compounds that have the capability to modulate $GABA_B$ receptor activity, said method comprising;
a) contacting cells expressing a functional $GABA_B$ receptor, wherein said cells do not normally express a functional $GABA_B$ receptor, with at least one reference compound, under conditions permitting the activation of the $GABA_B$ receptor;
b) contacting the cells of step a) with a test compound, under conditions permitting the activation of the $GABA_B$ receptor, and
c) determine whether said test compound modulates the $GABA_B$ receptor activity compared to the reference compound.

20. A method according to claim 19 wherein the capability of the test compound to modulate the $GABA_B$ receptor activity is determined using one or more of the functional responses selected form the group consisting of changes in potassium currents, changes in calcium concentration, changes in cAMP and changes in GTPγS binding

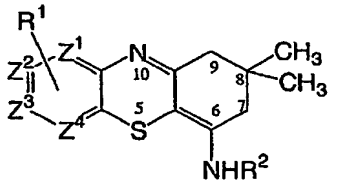
21. A method for identifying compounds that have the capability to modulate $GABA_B$ receptor activity, said method comprising;
a) contacting a membrane fraction of the cells according to claim 5, with the compound to be tested in the presence of radiolabeld GTPγS, under conditions permitting the activation of the $GABA_B$ receptor; and
b) determine GTPγS binding to the membrane fraction,
where an increase in GTPγS binding in the presence of the compound is an indicaton that the compound activates the $GABA_B$ receptor activity.

22. A method for identifying compounds that have the capability to modulate $GABA_B$ receptor activity, said method comprising;
a) contacting a membrane fraction of the cells according to claim 5, with the compound to be tested in the presence of radiolabeld GTPγS, under conditions permitting the activation of the $GABA_B$ receptor; and
b) determine GTPγS binding to the membrane fraction,
where an decrease in GTPγS binding in the presence of the compound is an indicaton that the compound inactivates the $GABA_B$ receptor activity.

23. A method according to claims 21 or 22 wherein the conditions permitting the activation of the $GABA_B$ receptor comprise the presence of a $GABA_B$ receptor agonist.

24. A method according to claim 23 wherein the $GABA_B$ receptor agonist is selected from the group consisting of GABA, baclofen and 3-APPA.

25. Use of a compounds of formula (I)



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein;
$=Z^1-Z^2=Z^3-Z^4=$ represents a divalent radical selected from the group consisting of
=N-CH=CH-N= (a), =N-CH=N-CH= (b), =CH-N=CH-N= (c)
=CH-CH=CH-CH= (d), =N-CH=CH-CH= (e), =CH-N=CH-CH= (f),
=CH-CH=N-CH= (g) and =CH-CH=CH-N= (h);
R^1 represents hydrogen, halo, hydroxyl, cyano, C_{1-6}alkyl, CF_3, amino or mono- or di(C_{1-4}alkyl)amino;
R^2 represents hydrogen, C_{1-6}alkyl or hydroxycarbonyl-C_{1-6}alkyl-, in the manufacture of a medicament for the treatment of an indication such as stiff man syndrome, gastroesophogeal reflux, neuropathic pain, incontinence and treatment of cough and cocaine addiction.

26. Use of a compound of formula (I) in the manufacture of a medicament to reduce transient lower esophagal sphincter relaxations (TLESR).

27. A compound of formula (I) wherein $=Z^1-Z^2=Z^3-Z^4=$ represents (a), (b) or (d), more preferably those compounds of formula (I) wherein $=Z^1-Z^2=Z^3-Z^4=$ represents (d).

28. A compound according to claim 27 for use as a medicine.

29. Use of a compound according to claim 27 in the manufacture of a medicament to reduce transient lower esophagal sphincter relaxations (TLESR).